J. Sleep Res. (2012) Regular Research Paper

Information content in cortical spike trains during brain state transitions

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Keywords
awake, brain states, entropy, firing rate, information, sleep, spike train

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Accepted in revised form 19 May 2012; received 8 December 2011

DOI: 10.1111/j.1365-2869.2012.01031.x

SUMMARY

Even in the absence of external stimuli there is ongoing activity in the cerebral cortex as a result of recurrent connectivity. This paper attempts to characterize one aspect of this ongoing activity by examining how the information content carried by specific neurons varies as a function of brain state. We recorded from rats chronically implanted with tetrodes in the primary visual cortex during awake and sleep periods. Electroencephalogram and spike trains were recorded during 30-min periods, and 2–4 neuronal spikes were isolated per tetrode off-line. All the activity included in the analysis was spontaneous, being recorded from the visual cortex in the absence of visual stimuli. The brain state was determined through a combination of behavior evaluation, electroencephalogram and electromyogram analysis. Information in the spike trains was determined by using Lempel–Ziv Complexity. Complexity was used to estimate the entropy of neural discharges and thus the information content (Amigó *et al. Neural Comput.*, 2004, 16: 717–736). The information content in spike trains (range 4–70 bits s^{-1}) was evaluated during different brain states and particularly during the transition periods. Transitions toward states of deeper sleep coincided with a decrease of information, while transitions to the awake state resulted in an increase in information. Changes in both directions were of the same magnitude, about 30%. Information in spike trains showed a high temporal correlation between neurons, reinforcing the idea of the impact of the brain state in the information content of spike trains.

INTRODUCTION

Information theory has previously been used to quantify how much information a neural response carries about external stimuli, for example in Rieke *et al.* (1998). However, not all neuronal discharges relate to such external stimuli. Recurrent circuitry within different brain areas itself generates activity even in the absence of external information, for example during sleep or during resting states in the awake there is spontaneous or emerging activity. Indeed, during slow-wave sleep there is a decrease in general brain activity (Maquet *et al.*, 1997; Schredl *et al.*, 2009); however, activity in primary and secondary sensory cortices appears to occur nevertheless (Braun *et al.*, 1997). Even though during sleep the cortex is functionally disconnected from external sources of stimuli, there is a level of activity in some areas of the cerebral cortex that is comparable to that occurring during the alert state.

Thalamocortical activity during non-rapid eye movement (NREM) sleep is dominated by the occurrence of different oscillatory activities (Steriade, 2003). Information is a measure of the uncertainty or novelty of the event being observed, the information being higher the more unlikely the event. Hence, from an information theory point of view, a highly regular and rhythmic neuronal discharge would transmit a small amount of information. This raises the question of how the information carried in cortical spike trains generated by the same neurons varies between sleep and alert states. To investigate this issue we have measured the information content in cortical spike trains over a specific set of neurons in a chronically implanted animal, and compared

the results between periods when the animal is alert and asleep. Comparisons across different awake–sleep–awake transitions reveal that information content in spike trains during awake states is usually higher than during sleep.

MATERIALS AND METHODS

Experiments

Recordings were obtained from one male Lister Hooded rat (400 g at implantation and testing) chronically implanted with tetrodes in the primary visual cortex.

Surgical procedure

Anesthesia was induced using intraperitoneal injections of ketamine (100 mg kg^{-1}) and xylacine (10 mg kg^{-1}). Rats were cared for and treated in accordance with the Spanish regulatory laws (BOE 256; 25-10-1990), which comply with the EU guidelines on protection of vertebrates used for experimentation (Strasbourg 3/18/1986).

The microdrive and tetrodes were mounted to the stereotaxic frame and the tetrodes lowered slowly 200 μm below the pia at V1 coordinates. All the recordings were obtained between 350 and 1000 μm depth. Reconstruction of the electrode track after performing anatomy of the animal confirmed that the recordings were obtained in V1. All details concerning electrophysiological recordings with the same system but in the auditory system can be found in Abolafia *et al.* (2011).

Electrophysiological recordings

After a post-operative recovery period (7 days) the recording sessions started. Over the course of 4–5 days, the electrodes were advanced in steps of 50 μm until spikes of 100–150 μV amplitude were obtained. Signals were amplified 15 000–35 000 times and high-pass filtered (360 Hz). Waveforms of identified spikes were sampled at 48 kHz (50 points per channel, 1 ms; 200 μs pre-threshold; 800 μs post-threshold), time-stamped and stored for off-line analysis. These spikes were the ones used for subsequent off-line spike sorting analysis. An electroencephalogram (EEG) was recorded single-endedly from one of the electrodes, low-pass filtered at 125 Hz cutoff, sampled at 250 Hz and stored with the unit data.

Cluster cutting

Isolating single units from the multiunit recording data was performed using Off-line sorter (Plexon, Dallas, TX, USA). Waveforms were first sorted by using the valley-seeking algorithm (Koontz and Fukunaga, 1972). Waveforms were considered to have been generated by a single neuron when they occurred simultaneously in the four electrodes of the tetrode, defining a discrete cluster in 3D principal component (or peak to peak) space distinct from clusters for other units using a multivariate analysis of variance test. Single units exhibited a recognizable refractory period (>1 ms) in their inter-spike interval histograms, and had a characteristic and distinct waveform shape and peak-to-peak amplitude when compared with other spikes.

Electromyogram (EMG) recordings

Recordings were obtained after the animal was implanted with a monopolar hook electrode (bare ≈ 1 mm at the tip) made of Teflon-coated stainless steel wire (50 μm diameter) in the neck muscles to record the EMG. The EMG was low-pass filtered at 500 Hz cutoff and sampled at 4800 Hz. EMG was not obtained in all cases.

Behavior monitoring with an infrared camera

The experimental animal was housed in large transparent Plexiglas cages (Rody Cavia, Savic, Heule, Belgium; 70 × 45 × 31 cm) with food and water available *ad libitum*. The rats were kept on a 12 h light/dark schedule. A well-trained experimenter coded the behavioral states by inspection of behavior. Four behavioral states were coded: (1) active exploration (locomotion, whisking, sniffing); (2) quiet waking, the animal was immobile (standing or sitting quietly) or engaged in automatic stereotyped behaviors (eating, drinking and grooming); (3) animal immobile and standing with rhythmic whisker movements; and (4) sleeping: the animal was lying immobile curling with eyes closed.

All the recordings were carried out in complete darkness with an infrared camera. Darkness was used in order to prevent visual stimulation during the awake states, and to restrict the activity to the spontaneously evoked one. During the recording session the animal remained in his own home cage and was free to move.

The duration of each recording session was between 20 and 30 min. If the session started with the animal sleeping (as in 4) during the recording, the experimenter entered into the recording room to wake up the rat, in order to evoke a sleep to awake transition.

Analysis of EEG/EMG

In order to detect sleep/awake stages an algorithm was used. Data were analysed in 5-s epochs with a sampling frequency of 250 Hz for EEG and 4800 Hz for EMG. The EEG and EMG signals were subject to simple amplitude analysis in the time domain. The EEG signal was filtered into the following five frequency bands of interest: delta (δ: 1.5–6 Hz); theta (θ: 6–10 Hz); alpha (α: 10.5–15 Hz); beta (β: 22–30 Hz); and gamma (γ: 35–45 Hz). Amplitudes (μV_{rms}) of the filtered data (EMG and each EEG band) were analysed. The root-mean-square (RMS) amplitudes of the EMG were used as the input for the first step of the algorithm. The EEG amplitudes (μV_{rms}) for each frequency band were combined into the following ratios. Let

$$P_1 = \frac{\delta \cdot \alpha}{\beta \cdot \gamma} \text{ and } P_2 = \frac{\vartheta^2}{\delta \cdot \alpha} \quad (1)$$

Then, the parameter P_1 provides discriminates between NREM sleep and the other states, and the parameter P_2 identifies REM sleep, as in Maloney *et al.* (1997) and Veasay *et al.* (2000).

Protocols

The algorithm works by comparing the incoming data with threshold values. EMG_{rms} amplitude provided a good discrimination between wakefulness and sleep, and was set as the first step. Ratios of EEG frequency band amplitudes were chosen that maximized discrimination between the different vigilance states. The NREM sleep was established by means of parameter P_1, conforming the second step. Finally, in the third step, REM sleep was identified using P_2.

The following analysis was carried out on the data (Louis *et al.*, 2004).

1. If EMG_{rms} amplitude was greater than threshold (T_1), the state was defined as awake and moving and sub-threshold amplitude was defined as sleep or quiet wake.
2. For epochs with sub-threshold EMG_{rms} amplitude, the parameter P_1 was computed and compared with its threshold (T_2). Epochs in which this parameter was above threshold T_2 were classified as NREM sleep and the remainder were classified as REM sleep.
3. If the EMG signal was poor or unavailable, the first step was omitted, and then the parameters P_1 and P_2 establish the state.
4. The third step uses the parameter P_2. Epochs with a suprathreshold T_3 were scored as REM sleep and the remainder were classified as quiet wake.

The large majority of the transitions between states included in the results were evaluated by the EEG analysis plus the evaluation of the behavior. In some cases the EMG was not recorded, and therefore we only include transitions between NREM sleep and awake state if the animal was moving in the awake. In this way we exclude cases when the animal could go into REM sleep. In some of the experiments the EMG was also recorded. These cases were useful to validate the ones in which only EEG and behavior were taken into account (Fig. 1).

Quantification of information content

The concept of information

Information in the central nervous system is transmitted between neurons by discrete, identical electrical pulses called action potentials (spikes). In fact, to find the mutual information between stimuli and neuron outputs (Borst and Theunissen, 1999), one must extract from the total information transmitted by the neuron, the so-called conditional information or 'noise' entropy, which quantifies the variability to repeated presentations of the same stimulus (Reinagel and Reid, 2000). However, even in the absence of (external) stimuli, there is ongoing activity in the cortex as a result of recurrent connectivity. Here we concentrate on the estimation of the total information (including local 'noise' information) carried by the spike trains generated by single neurons rather than on the estimation of the information conveyed by the neurons about a particular kind of stimuli.

Shannon Information Theory provides a mathematical framework for analysing information transmission in communication systems. If X is a discrete random variable with probability function $p(x_i)$, $i = 1, 2, ..., n$, then the information conveyed by the event $X = x_i$ is equal (in units of bits) to $-\log_2 p(x_i)$. The average information transmitted by the different realizations of X,

$$H(X) := -\sum_{i=1}^{n} p(x_i) \log_2 p(x_i) \quad (2)$$

is called the entropy of X (in bits).

If instead of a single random variable, we have a sequence $X = X_1X_2 ... X_n ...$ of random variables, then we are in the realm of the stochastic processes. Consider 'words' $x_1^l := x_1x_2 ... x_l$ of length l output by a process X assumed stationary for the time being, with 'letters' x_i taken from an 'alphabet' $A = \{a_1,..., a_d\}$. With $p(x_1^l)$ denoting the probability

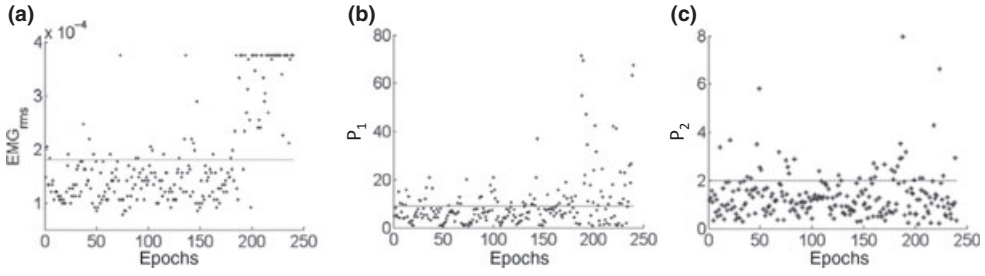

Figure 1. EEG and EMG analysis to determine brain states. The threshold was determined to be the point where the separation between states was maximal. Thresholds are indicated by the dotted lines. (a) EMG_{rms} amplitude versus epochs. (b) NREM ratio amplitude, P_1 versus epochs. (c) The plot shows those epochs that were below threshold in both plots (a) and (b). EMG, electromyogram.

for the length-l word x_1^l to occur, the block entropy of order l in units of bits is

$$H(l) = -\sum p(x_1^l)\log_2 p(x_1^l) \quad (3)$$

where the sum is over all words x_1^l. The entropy rate $h(X)$ is defined as

$$h(X) = \lim_{l\to\infty} \frac{1}{l} H(l). \quad (4)$$

Stationary stochastic processes are equivalently called information sources. We will consider the more general case of locally stationary sources. A process is locally stationary if it can be considered stationary most of the time, except for comparatively short transition phases between stationary states. Locally stationary sources can be assigned a slowly-changing, time-dependent entropy rate outside the transition phases by means of sliding time windows of adequate length.

A spike train, being a sequence of real numbers, generally corresponding to the absolute times of the spike occurrences, is not a discrete signal but an analog one. Once a spike train has been digitalized, it can be viewed as having been emitted by 'an information source' comprising everything preceding the emission (Amigó *et al.*, 2003; Crumiller *et al.*, 2011; Quiroga and Panzeri, 2009; Szczepanski *et al.*, 2011).

Codification

Here we used the binary temporal coding (Rieke *et al.*, 1998). Thus, every unit time interval of the spike train is divided into q small time bins $\Delta\tau$ (depending on the desired observation precision), and the digits 0 or 1 are assigned to each time bin according to whether no (0) or at least one (1) spike has occurred (Fig. 1 in Amigó *et al.*, 2004). Such a sequence of bits can then be treated as a trajectory of a stochastic process.

To extend this method to locally stationary signals we use a sliding window $[t, t + T]$. T is chosen such that: (1) it is long enough so as to estimate the entropy rate with a good accuracy; and, at the same time (2) it is short enough to guarantee the approximate stationarity of the signal. This trade-off has to be checked on a case-by-case basis. Given the window and the encoding frequency $f = 1/\Delta\tau$, a spike train is represented at time t by a bit sequence of length fT.

In order to obtain the information rate conveyed by the neurons, the parameters in the scheme above must be chosen appropriately: (1) the encoding frequency f; and (2) the length of the sliding time window T. We chose $f = 80$ Hz, as the saturation levels we observed in Szczepanski *et al.* (2003) were set at this value, so the further increase of f does not affect the information rate. Moreover, in our experiments the maximal local firing rate was never larger than 25 spikes s^{-1}, and therefore with the binning used there is a very low probability that more than one spike falls into a single bin. Our experimental data corroborate this fact. In order to satisfy quasi-stationarity and still preserve good accuracy of the entropy rate estimation we assumed $T = 5$ s.

Entropy estimators: complexity

The main problem in estimating the entropy rate of neural responses is the small size of the samples. Thus, different entropy rate estimators have been proposed (Gao *et al.*, 2003). The basic requirements of these estimators are stationarity and ergodicity of the underlying stochastic process.

In our previous research (Amigó *et al.*, 2004; Szczepanski *et al.*, 2003) we used Lempel–Ziv Complexity (LZC), as defined in Lempel and Ziv (1976).[1] For a given sequence of n symbols, LZC counts the number of new patterns that appear along the sequence.

For an ergodic source, the normalized LZC of a given output estimates its entropy rate with probability 1 (Ziv, 1978). In the case of neurophysiological data, it was shown in Amigó *et al.* (2004) that LZC provides estimations of the entropy rate similar to the estimator of Strong *et al.* (1998).

RESULTS

Recordings from 52 neurons were included. In this study we concentrated on the analysis of neuronal activity in terms of the amount of information transferred. The average firing rates in our experiment were between 4 and 10 spikes s^{-1}. We analysed:

– The influence of the cluster cutting method.
– Awake–sleep and sleep–awake transitions.
– Relation between the firing rate during spike trains and the corresponding information content.

Restrictive and non-restrictive cutting

The relation between the amount of information and firing rate is affected by the cutting of clusters in order to separate spikes originating in different neurons. To evaluate the influence of how conservative the cluster cutting was, the same spike trains were cut with different restriction levels. Clusters of spikes were separated as explained in the Materials and methods. To carry out a more strict clustering, the centroid and sigmas of the cloud of points corresponding to each cluster were calculated in 3D principal component space. Outliers were removed when they were further than either 1.3 SD ($n = 14$ recordings, $n = 6$ neurons) or 2 SD ($n = 37$ recordings, $n = 8$ neurons) by measuring the Mahalanobis distance (Offline Sorter, Plexon). Two distinct subsets of cells were considered.

[1]The concept of complexity we use is related but not identical to one developed later (Ziv, 1978) that is widely implemented in information technologies for lossless data compression (e.g. WinZip, PK-Zip).

As is shown in Fig. 2, the average information is higher in the spike trains that were recorded without, rather than with, removal of outliers. However, we found information rates before and after the removal of outliers highly correlated. This result shows that our relative measurements during sleep and awake transitions should not be influenced by the cutting of the clusters, and therefore we did not further use removal of outliers tool.

Characteristics of the rates of information during awake–sleep–awake transitions

Thirty-four neurons were recorded while they went through transitions awake–sleep or *vice versa*. For these neurons, we estimated the average information content for the sleep state and awake state as the result of the average information during windows of 5 s before and after the transition (400 values). The values of information in spike trains during the awake state ranged between 4.3 and 77.5 bits s^{-1}, with an average of 32.0 ± 14.2 bits s^{-1} (n = 34 neurons; x ± SD). The values during sleep ranged between 3.5 and 74.3 bits s^{-1}, with an average of 22.0 ± 13.0 bits s^{-1} (n = 34; x ± SD). In 15 neurons the transition from sleep to awake state was characterized. In 13 of them there was an increase of information in the spike trains, in one remained constant and in one it decreased. The increase was from an average of 19.1 ± 8.8 (sleep) to 28.0 ± 11.6 bits s^{-1} (awake; n = 15; Fig. 3). In 19 neurons a transition from awake to sleep was recorded. In all of the cases there was a decrease in the spike trains information content, which was from an average of 35.1 ± 16.0 (awake) to 24.2 ± 15.4 bits s^{-1} (sleep; n = 19). The two blocks of measurements (15 and 19 cells) obtained for sleep and for awake of information were not statistically different (t-test; P = 0.15 for awake and P = 0.26 for sleep). In both cases the values during a standard paired t-test show that there is a highly significant difference between the means of the transitions (P < 0.01) both from sleep to awake and *vice versa*. Similarly a non-parametric paired sign test also rejects the hypothesis of equal medians (P < 0.01) in favor of the hypothesis that the median of information during the awake state is greater than that during sleep state (Fig. 3).

These transitions can also be seen explicitly over the time evolution (Fig. 4). We consider two of the most interesting physiological behaviors. The brain states are shown as a balance between behavior evaluation and EEG slow-wave activity analysis. In Fig. 4a the rat alternated several times between the states of sleep and awake. The correspondence between these states and the low and high information rates are obvious. In Fig. 4b the rat remained in deep sleep and then was woken up abruptly. Here this transition process is also well reflected in the corresponding increase of the information rate. Information rates for two neurons are presented. Interestingly the fluctuations in both states are similar.

Next we estimate the correlation of the information content in two pairs of neurons. The first pair consists of closely located neurons recorded by the same tetrode, while the second one consists of more distant neurons recorded by two separate tetrodes. The estimated correlation values (Fig. 5) for both cases shows that the pair of closer located neurons is twice as correlated than a pair of more distant neurons. We have observed this in a few cases, but so far we cannot make

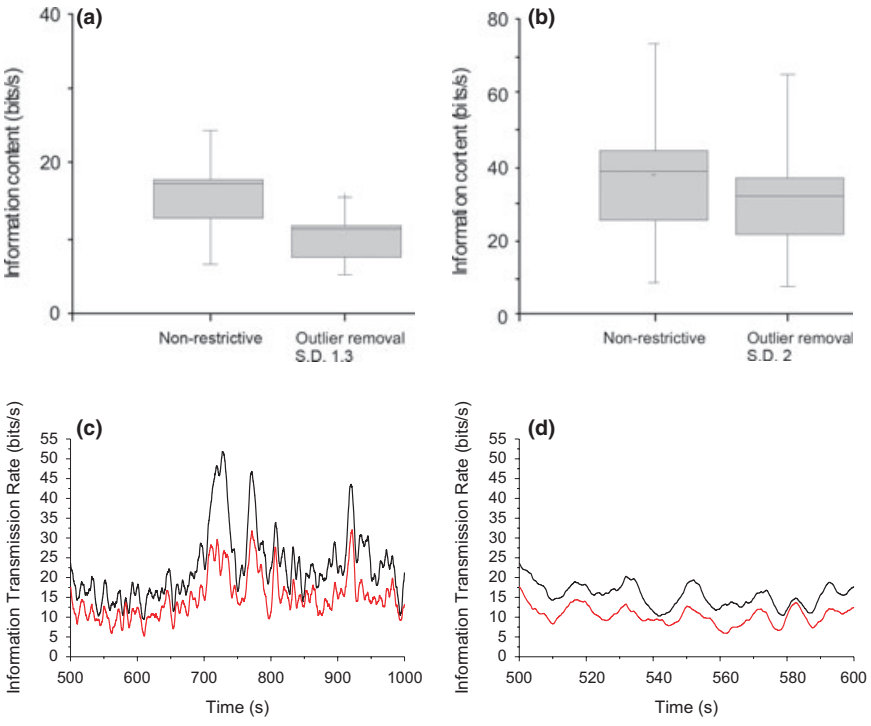

Figure 2. Information content in more versus less restrictive cluster cutting. Two distinct subsets of cells are presented. (a) Average information content in six neurons for a cluster cutting with no outlier removal and for removal of those further away than 1.3 SD. (b) Average information in eight neurons for a cluster cutting with no outlier removal and for removal of those further away than 2 SD. (c) Information content over time in a spike train whose spikes have been isolated without (non-restrictive) and with (restrictive) removal of outliers. Long time range is presented. (d) The same, but for short time range.

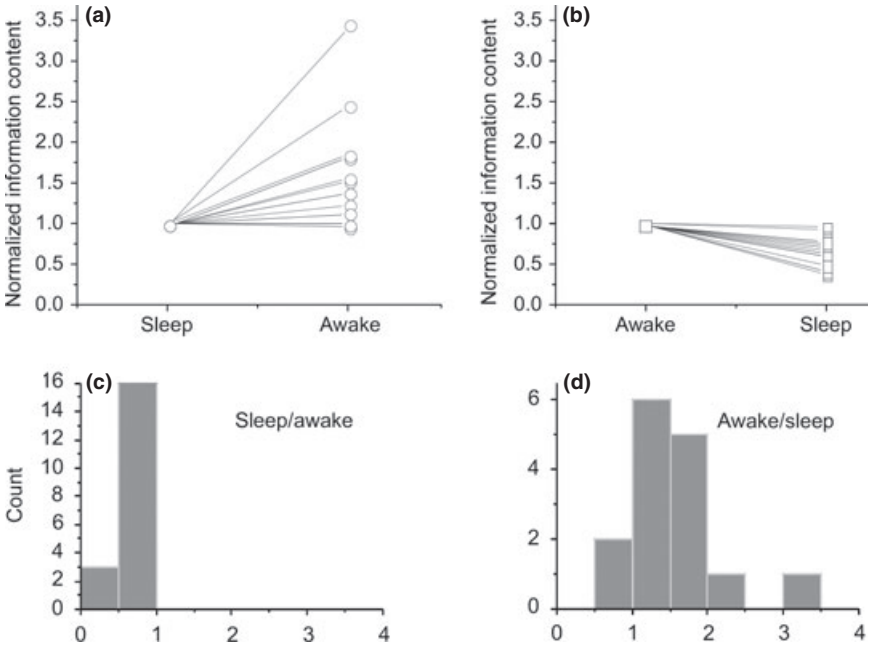

Figure 3. Information content variations in sleep/awake and awake/sleep transitions. (a) Normalized values of information content in 15 transitions from sleep to awake. The awake values were divided by the preceding sleep values. (b) Same as in (a) but for 19 awake to sleep transitions. (c) During transitions from awake to sleep, the values for each neuron in the final state (sleep) were divided by the ones during the preceding awake state (n = 19). (d) During transitions from sleep to awake, the values for each neuron in the final state (awake) were divided by the ones during the preceding sleep state (n = 15).

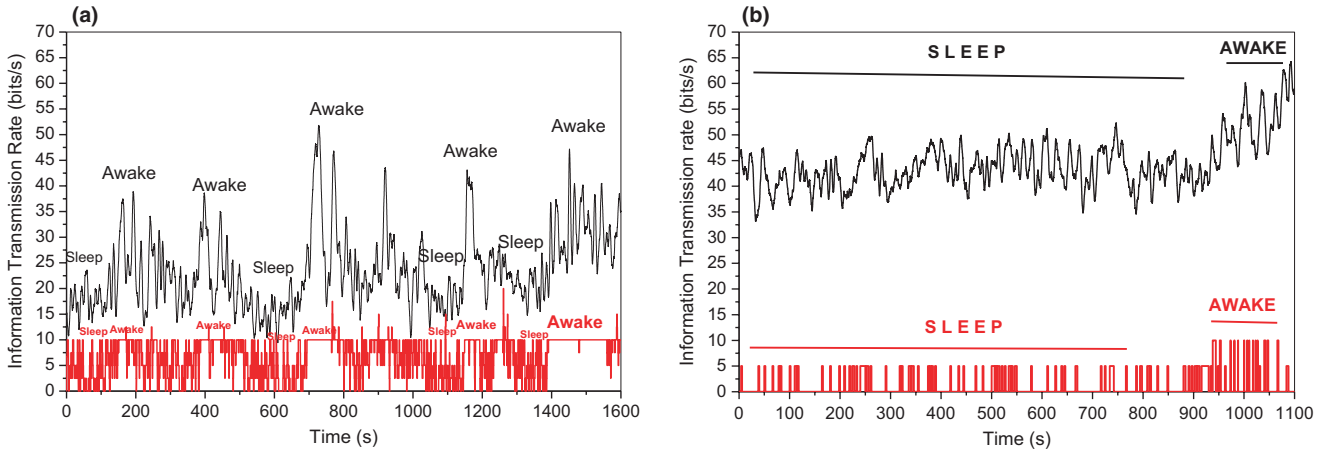

Figure 4. Typical runs of the information rate for two neurons are presented. The awake–sleep transitions for two typical physiological states as a function of time. (a) The rat alternated several times between the states of sleep and awake. (b) The rat remained in the deep sleep, and then suddenly was waken up. The brain states classification by EEG (red line) is also presented. In our plot the awake state corresponds to the value of 10.

a systematic description of the relationship between correlation in information content and neuronal distance.

Mathematically, the question arises whether the locally stationary neural activity can be modeled as surrogated data generated by a non-homogeneous Poisson process with parameter $\lambda(t)$ (in fact the local firing rate) taken from the experimental data. This problem will be analysed in detail in a separate study.

Firing rate and information content in spike trains

As established in classical physiology, the firing rate is most often related to the stimulus intensity, i.e. the firing rate increases with increasing stimulus intensity. Understanding the relationship between information and the firing rate is a highly relevant question (Rieke *et al.*, 1998; Churchland *et al.*, 2010).

To test the hypothesis as to whether the increase of firing rate leads always to an increase of information content, we compared the information rates with corresponding firing rates. We collected the information and firing rates from a 5-s time window moving over the whole time range of the experiments. Our results are presented in Fig. 6. In order to compare the time evolution of firing rates and information rates we calculated the Pearson linear correlation coefficients of these two quantities. We observe that the correlation is always positive. On the other hand, our results show that although in the awake state this coefficient is relatively high

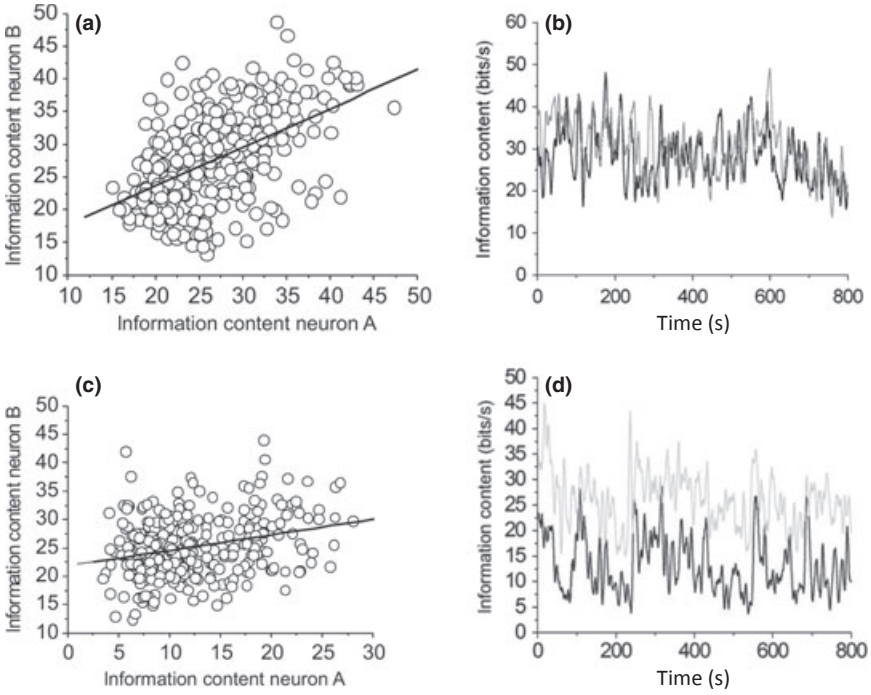

Figure 5. Correlation of information content in spike trains of neighboring neurons. (a) Correlation of information between two neurons recorded with the same tetrode, and therefore closely located. Correlation has an R of 0.5 and $P < 0.0001$. (b). Information content of both neurons (A and B) in black and gray, respectively. (c). Correlation of information content between two neurons recorded with two different tetrodes and therefore not so closely located. Correlation has an R of 0.27 and $P < 0.0001$. (d) Information content of both neurons (A and B) in black and gray, respectively.

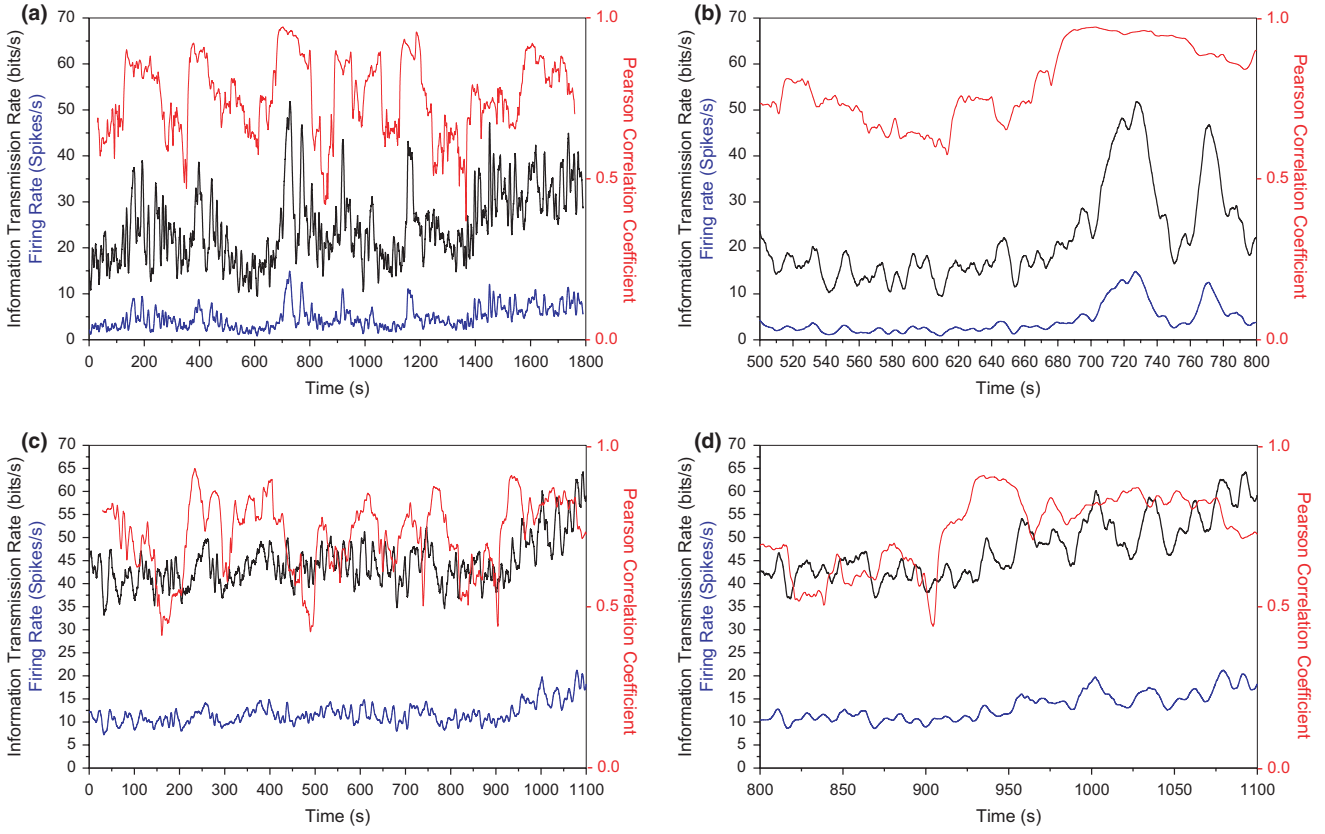

Figure 6. Comparison of information transmission and firing rates. (a) The case for the less active neuron, the average firing rate is equal to 4 spikes s^{-1}. Information transmission rate is depicted by a black line, local firing rates by a blue line, while their Pearson correlation coefficient is depicted by a red line. The average value of Pearson correlation coefficient for the awake state is 0.60 ± 0.05, while for the sleep state it is 0.49 ± 0.07. (b) The same as in (a), but for short time range. (c) Information transmission rate for a more active neuron, with an average firing rate equal to 10 spikes s^{-1}. Here the average value of Pearson correlation coefficient for the awake state is 0.58 ± 0.03 and for the sleep state is 0.49 ± 0.08. The local firing rates in our experiments never exceed 20 spikes s^{-1}. Observe the existence of the time intervals (especially for the sleep periods) of the significant deviation of the Pearson coefficient from 1. This coefficient was estimated locally using a 1-min-long sliding window (4800 bits).

(above 0.85), in the sleep states it is much lower, even below 0.5 (Fig. 6). The significant deviation of the Pearson coefficient from 1 undermines the hypothesis of permanent linear relation (Feller, 1958) between information and firing rates. The lack of linearity is not surprising. Although the essence of the Shannon information rate is probabilistic, it turns out that the repeating patterns in the encoded message play a crucial role in estimating the entropy. It is known that the advanced entropy estimators measure the evolution of patterns along a sequence, especially visible for the complexity-like estimators. Our observation corroborates the fact that the information included in spike trains depends in a very subtle way on the structure of spike patterns and not just only a simple characteristic such as the firing rate. This fact is well demonstrated in the intervals (200 s, 300 s), (500 s, 650 s) in Fig. 6a, and (150 s, 200 s), (450 s, 500 s) in Fig. 6c.

DISCUSSION

Our results show that transitions from awake to sleep and from sleep to awake resulted in similar changes in information content in the spike trains (about 10 bits s^{-1} both for decrease and increase). A typical characteristic of the information transmission during the transition process is for there to be large fluctuations, meaning that the transmission takes place in packages (there are short intervals with small information rate alternating with short intervals with high information rate). During awake states the average value of information in spike trains was higher than during slow-wave sleep states (a change of 5.3 ± 0.8%). This is a moderate change and suggests that even though it is rhythmic, neuronal activity during slow-wave sleep has a relatively high information content per spike. This seems to be concomitant with the fact that during slow-wave sleep activity there is high spatial correlation and long time scale dynamics (Destexhe *et al.*, 1999). Our results suggest that during sleep neurons rather use a smaller number of spikes with higher variability of inter-spike intervals than use more spikes; this strategy could be to minimize the energy needed to transmit the same information as each spike has an energy cost (Lennie, 2003) and therefore its existence must be relevant to the system. The significant (Fig. 6) deviation of the Pearson coefficient from 1 and the strongly fluctuating information rate per spike show that a given amount of information can be transmitted by both a smaller number or larger number of spikes. On the other hand in the same figure, for lower spike rates we can observe a unique (one-to-one) correspondence to information rates, a fact that can be explained also in terms of energy saving (a smaller number of spikes, which in fact are more frequent and use less energy, can transmit different amount of information). These observations indicate that the neuronal coding process is much more subtle than the straightforward transmission of information directly via firing rate.

It is also clear that it is not only information within spike trains that varies between brain states. Organized activity, such as the occurrence of slow oscillations, is also highly regular in deep anesthesia, while it becomes stochastic in light anesthesia (Deco *et al.*, 2009). We could speculate on the brain mechanisms contributing to the generation of higher information content in spike trains during the awake than in sleep, or higher stochasticity of population events. Even though it is not critical, as has been already discussed, an increase in firing rate during the awake state could be a contributing factor. Further, we should consider temporal correlations as a mechanism decreasing information transmission rate. Closely located cells, in particular the connected ones, show higher long time scale correlations than cells further away, a difference that is more obvious during sleep both in the cortex (Peyrache *et al.*, 2012) and hippocampus (Hirase *et al.*, 2001). Spike correlations are also higher during spontaneous than in sensory-evoked activity (Berger *et al.*, 2007; Smith and Kohn, 2008). However, it has been as well described that recurrent networks like the cortical network are able to generate asynchronous states even during spontaneous activity with neurons presenting near-zero mean correlations (Renart *et al.*, 2010). Finally, we should also consider the brain functional connectivity in both states. While in slow-wave sleep there is a dominance of local connectivity, a functional network involving long-distance connections is characteristic of the awake state (Massimini *et al.*, 2005; Spoormaker *et al.*, 2011). The different networks contributing to the resulting emerging activity could contribute to the different information content in spike trains in different brain states.

ACKNOWLEDGEMENTS

This paper has been supported (Janusz Szczepanski, Eligiusz Wajnryb) by Polish National Science Centre grant N N519 646540, and by the Spanish Ministry of Science and Innovation to Maria V. Sanchez-Vives (BFU2008-01371 and BFU2011-27094). Jose M. Amigo was supported by the Spanish Ministry of Science and Innovation, grant MTM2009-11820.

CONFLICT OF INTEREST

All authors have no conflict of interests with organization(s) with a financial interest in the subject matter of the paper, or any actual or potential conflict of interest.

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